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(81) 指定国
AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MN, NO, NZ, PL, RO, RU, SI, SK, TJ, TT, UA, US, UZ, VN, 欧州特許(AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI特許(BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG), ARIPO特許(KE, MW, SD, SZ).

添付公開書類 国際調査報告書
補正書

(54) Title : GENE SIGNATURE

(54) 発明の名称 ジーン・シグナチャー

(57) Abstract

A 3'-directed cDNA library which accurately reflects the abundance ratio of mRNA in a cell has been prepared from various human tissues, and sequencing of the cDNAs contained in the library has been conducted to examine the incidence of each cDNA in each tissue. As each cDNA has expression information with each tissue corresponding to the mRNA concentration, these cDNAs are usable as a probe or primer for detecting cell anomaly or discriminating cells. The cloned gene can produce proteins utilizable as a medicine or the like.

TAATCANTGT TATTGTGTTC CANTTTAACT GGGTTAAATG TTTN 284

配列番号：3190
配列の長さ：282
配列の型：核酸
トポロジー：直鎖状
クローン名：HUMGS03761
配列：
GATCTCGACT CCCCCCTGGC CACAGACCCC CAGGTCATTG TGTTCACTGT ACTCTGTGGG 60
CAAGGATGGG TCCAGAAGAC CCCACTTCAG GCACTAAGAG GGGCTGGACC TNTGCGGCAG 120
GAAGCCAAAG AGACTGGGCC TAGGCCAGGA GTTCCCAAAT NTGAGGGGCG AGAAACAAGA 180
CAAGCTCCTC CCTTGAGAAT TCCCTGTGGA TTTTTAAAAC AGATATTATT TTTNTNATTA 240
TTGTGACAAA ATGTTGNTAA ATGGGATATT AAATAGAATA AA 282

配列番号：3191
配列の長さ：279
配列の型：核酸
トポロジー：直鎖状
クローン名：HUMGS03762
配列：
GATCTGGAGA AGTAAGATGG CCAAATAAAA GCCTCTACCA ATCATCCTCC CCACAGGAAC 60
ACCAAATTTA AGAACTATCT ACACAAAAAA GCACCTTCAT AAGAACCAAA AATCAGAGAG 120
AACAAGGATA AAGAAGTATC CAAATACAAA GAAAATGTTA TGCAAGTGAC CTTTAGAGAT 180
GTTTTAAAGA TGACAAAATA TTGATGANGA TGGGCCAACA AGTGTTACTG TTACCTCTAA 240
TAAAGTTTCA TCACTAGTTT CACCATGGTT AATTGGAAA 279

配列番号：3192
配列の長さ：277
配列の型：核酸
トポロジー：直鎖状
クローン名：HUMGS03763
配列：
GATCTGCTCA AATGCACCAA CACTGCCAAG TGACTAAGGT AGAAAAGAAA AATAACAGGT 60
ATCGTCATCT GAAGGACAGA TGAATCTTTT TCTGCCCCTT CTTCACAATG GAATATAAGG 120
AACAATTATG GGATGTCATC AGAATGGATG CCATAGGACC TACAGCTCCC TTTCTNTTTA 180
TTGTNATTAT ACTTTAAATA TGACATTGTC TTTNATGTGT ATGTTCCTAT ATTTTCAATG 240
TATCTTTTTC CTTCAGTAAA CCTGATATTC AAATAAA 277

配列番号：3193
配列の長さ：277
配列の型：核酸
トポロジー：直鎖状
クローン名：HUMGS03764
配列：
GATCACAGGG AGCCTGTGTT TGTTGGAGGT GTTCCAGAAT CTNTACTGAC ACCACGCTTG 60

Page 1 (JEinsmann, 07/11/2000, EAST Version: 1.01.0013)

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Db    722 AGGAGCATCACCACACCTCCCTACCCCACCCCCACTCCTCCACCCCCTC-GCTGCTCCTT 780

Qy    953 GCTCCAGACCTGCCCCTCCCTCTAGAGGCTGCCTGGGCCTGTTCACGTGTTTTCCATCCC 1012

Db    781 GGTCCAGTCCTGTCTCTCC--TCAAAGGCAGCCAGAGCTTGTTCACATGTTTCCATTCC- 838

Qy   1013 ACATAAATACAGTATTCCCACTCTTATCTTACAACTCCCCCACCGCCCACTCTCCACCTC 1072

Db    838 ------ACAGACGTATCCTTGCTCTTCTTAACATCCCATCCCACCACAACTATCCACCTC 891

Qy   1073 ACTAGCTCCCCAATCCCTGACCCTTTGAGGCCCCCAGTGATCTCGACTCCCCCCTGGCCA 1132

Db    892 ACTAGCTCCCAAAGCCCCTAC--------------TTATCCCTGACTCCCCCACCCACT 936

Qy   1133 CAGACCCCCAGGGCATTGTGTTCACTGTACTCTGTGGGCAAGGATGGGTCCAGAAGACCC 1192

Db    937 CACCCGACCACGTGTTTATTGACTTTGTGCAC---------------------------- 969

Qy   1193 CACTTCAGGCACTAAGAGGGGCTGGACCTGGCGGCAGGAAGCCAAAGAGACTGGGCCTAG 1252

Db    969 -----CAGGCACTGAGATGGGCTGGACCTGGTGGCAGGAAGCCAGAGAACCTGGGACTAG 1023

Qy   1253 GCCAGGAGTTCCCAAATGTGAGGGGCGAGAAACAA-GACAAGCTCCTCCCTTGAGAATTC 1311

Db   1024 GCCAGAAGTTCCCAACTGTGAGGGGGAAGAGCTGGGGACAAGCTCCTCCCTGGA----TC 1079

Qy   1312 CCTGTGGATTTTTAAAACAGATATTATTTTTATTATTATTGTGACAAAATGTTGA 1366

Db   1080 CCTGTGGATTTTGAAA--AGATACTATTTTTATTATTATTGTGACAAAATGTTAA 1132
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RESULT   5
X23425
ID   X23425 standard; DNA; 701 BP.
AC   X23425;
DT   18-JUN-1999  (first entry)
DE   Mouse TNRL3 DNA.
KW   Tumour necrosis factor receptor; signal transducer molecule; TNF; APO4;
KW   developmental abnormality; gestational abnormalitity; prostate cancer;
KW   APO6; APO8; APO9; TNRL-1; TNRL-3; diagnosis; treatment; therapy; disease;
KW   cytoplasmic domain; immunogen; antibody preparation; breast carcinoma;
KW   apoptosis; mouse; ss.
OS   Mus sp.
FH   Key             Location/Qualifiers
FT   CDS             1. .636
FT                   /*tag= a
FT                   /product= "TNRL3"
PN   WO9911791-A2.
PD   11-MAR-1999.
PF   04-SEP-1998; U18393.
PR   05-SEP-1997; US-924634.
PA   (UNIW ) UNIV WASHINGTON.
PI   Chaudhary PM;
DR   WPI; 99-205191/17.
DR   P-PSDB; W93591.
PT   New Tumor Necrosis Factor family receptor polypeptides and ligands -
PT   useful for diagnosis and treatment of prostate cancer and
PT   developmental or gestational abnormalities
PS   Example VII; Fig 13B; 156pp; English.
CC   This invention describes isolated Tumor Necrosis Factor (TNF) family
CC   receptor polypeptides: APO4, APO6, APO8 and APO9 or their active
CC   fragments, and isolated TNF related ligands 1 and 3 (TNRL1 and TNRL3) or
CC   their active fragments. APO4 is useful for diagnosing prostate cancer
CC   by determining levels of APO4 in an individual. Prostate cancer can also
CC   be treated using APO4 selective binding agents linked to a therapeutic
CC   moiety. APO4 polypeptides are also useful for identifying selective
CC   binding agents, useful in diagnosis/treatment of disease by binding of
CC   agents to the polypeptide/active fragment which is extracellular, or
CC   expressed on the cell surface. The binding is preferably performed in
CC   vivo. APO4 polypeptides/ active fragments are also useful for screening
CC   for agonists and antagonists by binding and observing the changer in APO4
CC   activity. Effective pharmacological agents useful in diagnosis or
CC   treatment of disease are also identified using APO4 polypeptides/active
CC   fragments and APO4 signal transducer molecules that specifically interact
CC   with a cytoplasmic domain of APO4 and detecting a change in level of APO4
CC   activity. The method is performed in vivo or in vitro. APO polypeptides
CC   are all useful as immunogens for preparing antibodies. APO4 is also
CC   useful for diagnosis/treatment of developmental or gestational
CC   abnormalities. APO8 was transfected to human breast carcinoma cell line
CC   MCF-7, and induced apoptosis.
SQ   Sequence   701 BP;    139 A;    210 C;    203 G;    149 T;
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  Query Match           37.8%;  Score 519.2;  DB 1;  Length 701;
  Best Local Similarity  87.3%;  Pred. No. 1.8e-99;
  Matches  569;  Conservative    0;  Mismatches   83;  Indels    0;  Gaps    0;

Qy    220 CTGGCCGTGGTCAGTTTGGGGAGCCGGGCATCGCTGTCCGCCCAGGAGCCTGCCCAGGAG 279

Db      1 CTGGTCGTGGTCAGCCTGGGGAGCTGGGCAACGCTGTCTGCCCAGGAGCCTTCTCAGGAG 60

Qy    280 GAGCTGGTGGCAGAGGAGGACCAGGACCCGTCGGAACTGAATCCCCAGACAGAAGAAAGC 339

Db     61 GAGCTGACAGCAGAGGACCGCCGGGAGCCCCCTGAACTGAATCCCCAGACAGAGGAAAGC 120

Qy    340 CAGGATCCTGCGCCTTTCCTGAACCGACTAGTTCGGCCTCGCAGAAGTGCACCTAAAGGC 399

Db    121 CAGGATGTGGTACCTTTCTTGGAACAACTAGTCCGGCCTCGAAGAAGTGCTCCTAAAGGC 180

Qy    400 CGGAAAACACGGGCTCGAAGAGCGATCGCAGCCCATTATGAAGTTCATCCACGACCTGGA 459

Db    181 CGGAAGGCGCGGCCTCGCCGAGCTATTGCAGCCCATTATGAGGTTCATCCTCGGCCAGGA 240

Qy    460 CAGGACGGAGCGCAGGCAGGTGTGGACGGGACAGTGAGTGGCTGGGAGGAAGCCAGAATC 519

Db    241 CAGGATGGAGCACAAGCAGGTGTGGATGGGACAGTGAGTGGCTGGGAAGAGACCAAAATC 300

Qy    520 AACAGCTCCAGCCCTCTGCGCTACAACCGCCAGATCGGGGAGTTTATAGTCACCCGGGCT 579

Db    301 AACAGCTCCAGCCCTCTGCGCTACGACCGCCAGATTGGGGAATTTACAGTCATCAGGGCT 360

Qy    580 GGGCTCTACTACCTGTACTGTCAGGTGCACTTTGATGAGGGGAAGGCTGTCTACCTGAAG 639

Db    361 GGGCTCTACTACCTGTACTGTCAGGTGCACTTTGATGAGGGAAAGGCTGTCTACCTGAAG 420

Qy    640 CTGGACTTGCTGGTGGATGGTGTGCTGGCCCTGCGCTGCCTGGAGGAATTCTCAGCCACT 699

Db    421 CTGGACTTGCTGGTGAACGGTGTGCTGGCCCTGCGCTGCCTGGAAGAATTCTCAGCCACA 480

Qy    700 GCGGCCAGTTCCCTCGGGCCCCAGCTCCGCCTCTGCCAGGTGTCTGGGCTGTTGGCCCTG 759

Db    481 GCAGCAAGCTCTCCTGGGCCCCAGCTCCGTTTGTGCCAGGTGTCTGGGCTGTTGGCGCTG 540

Qy    760 CGGCCAGGGTCCTCCCTGCGGATCCGCACCCTCCCCTGGGCCCATCTCAAGGCTGCCCCC 819

Db    541 CGGCCAGGGTCTTCCCTTCGGATCCGCACCCTCCCCTGGGCTCATCTTAAGGCTGCCCCC 600

Qy    820 TTCCTCACCTACTTCGGACTCTTCCAGGTTCACTGAGGGGCCCTGGTCTCCC 871

Db    601 TTCCTAACCTACTTTGGACTCTTTCAAGTTCACTGAGGGGCCTTGCTCTCCC 652
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RESULT   6
T22190
ID   T22190 standard; cDNA to mRNA; 282 BP.
AC   T22190;
DT   27-AUG-1996  (first entry)
DE   Human gene signature HUMGS03761.
KW   Gene signature; messenger RNA; mRNA; relative abundance; frequency;
KW   human; cloning; mapping; non-biased library; diagnosis; detection;
KW   cell typing; abnormal cell function; ss.
OS   Homo sapiens.
PN   WO9514772-A1.
PD   01-JUN-1995.
PF   11-NOV-1994; J01916.
```

PR 12-NOV-1993; JP-355504.
PA (MATS/) MATSUBARA K.
PA (OKUB/) OKUBO K.
PI Matsubara K, Okubo K;
DR WPI; 95-206931/27.
PT Identifying gene signatures in 3'-directed human cDNA library - e.g.
PT for diagnosis of abnormal cell function, by preparing cDNA that
PT reflects relative abundance of corresp. mRNA in specific human
PT tissues
PS Claim 1; Page 1067; 2245pp; Japanese.
CC A single-stranded DNA (or its complementary strand or the corresp.
CC double-stranded DNA) which comprises one of the 7837 "GS" sequences
CC given in T19001-T26837 and which is able to hybridise to part of
CC human genomic DNA, cDNA or mRNA is claimed. The GS (Gene Signature)
CC sequences were obtained from 3'-directed cDNA libraries prepared
CC from various human tissues; synthesis of cDNA was initiated from the
CC 3'-end of mRNA by using poly(T) as the sole primer. Since the 3'-
CC untranslated sequence is unique to a particular mRNA species, almost
CC all the 3'-oriented cDNAs hybridise with specific mRNAs. Each library
CC is constructed so as to reflect accurately the relative abundance of
CC different mRNAs in the particular tissue from which it was derived.
CC The appearance frequency of a given GS in a cDNA library can be
CC determined (esp. using primers and probes derived from the GS
CC sequences) as a means of diagnosing abnormal cell function or for
CC recognising different cell types.
SQ Sequence 282 BP; 80 A; 62 C; 69 G; 66 T;

Query Match 17.9%; Score 245.4; DB 1; Length 282;
Best Local Similarity 97.3%; Pred. No. 1e-42;
Matches 257; Conservative 0; Mismatches 6; Indels 1; Gaps 1;

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Qy   1111 GATCTCGACTCCCCCCTGGCCACAGACCCCCAGGGCATTGTGTTCACTGTACTCTGTGGG 1170
          ||||||||||||||||||||||||||||||||| |||||||||||||||||||||||||
Db      1 GATCTCGACTCCCCCCTGGCCACAGACCCCCAGGTCATTGTGTTCACTGTACTCTGTGGG 60

Qy   1171 CAAGGATGGGTCCAGAAGACCCCACTTCAGGCACTAAGAGGGGCTGGACCTG-GCGGCAG 1229
          ||||||||||||||||||||||||||||||||||||||||||||||||||  |||||||
Db     61 CAAGGATGGGTCCAGAAGACCCCACTTCAGGCACTAAGAGGGGCTGGACCTNTGCGGCAG 120

Qy   1230 GAAGCCAAAGAGACTGGGCCTAGGCCAGGAGTTCCCAAATGTGAGGGGCGAGAAACAAGA 1289
          ||||||||||||||||||||||||||||||||||||||||| ||||||||||||||||||
Db    121 GAAGCCAAAGAGACTGGGCCTAGGCCAGGAGTTCCCAAATNTGAGGGGCGAGAAACAAGA 180

Qy   1290 CAAGCTCCTCCCTTGAGAATTCCCTGTGGATTTTTAAAACAGATATTATTTTTATTATTA 1349
          |||||||||||||||||||||||||||||||||||||||||||||||||| | ||||
Db    181 CAAGCTCCTCCCTTGAGAATTCCCTGTGGATTTTTAAAACAGATATTATTTTTNTNATTA 240

Qy   1350 TTGTGACAAAATGTTGATAAATGG 1373
          |||||||||||||||| |||||||
Db    241 TTGTGACAAAATGTTGNTAAATGG 264
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RESULT 7
X53491/c
ID X53491 standard; DNA; 114955 BP.
AC X53491;
DT 05-JUL-1999 (first entry)
DE Human adenosine A1 receptor antisense oligonucleotide fragment.
KW Antisense oligonucleotide; multiple target; antisense treatment;
KW impaired respiration; inflammation; lung disease;
KW pulmonary vasoconstriction; inflammation; allergic rhinitis;
KW acute asthma; allergy; asthma; impeded respiration;
KW respiratory distress syndrome; pain; cystic fibrosis;
KW pulmonary hypertension; pulmonary vasoconstriction; emphysema;
KW chronic obstructive pulmonary disease; leukemia; lymphoma; carcinoma;
KW colon cancer; breast cancer; lung cancer; pancreatic cancer;
KW hepatocellular carcinoma; kidney cancer; melanoma; hepatic metastasis;
KW prostate cancer; ss.
OS Synthetic.
PN WO9913886-A1.
PD 25-MAR-1999.
PF 17-SEP-1998; U19419.

PR 09-JUN-1998; US-093972.
PR 17-SEP-1997; US-059160.
PA (UYEC-) UNIV EAST CAROLINA.
PI Nyce JW;
DR WPI; 99-229400/19.
PT New antisense oligonucleotides used in treatment of, e.g. pulmonary
PT vasoconstriction
PS Disclosure; Page 37; 120pp; English.
CC The specification describes antisense oligonucleotides (X52869-X55271)
CC directed against at least 2 mRNAs selected from target genes, coding and
CC non-coding regions of RNAs corresponding to target genes, gene
CC initiation codons, genomic flanking regions, intron-exon borders, the
CC 5'-end, the 3'-end and the juxta-section between coding and non-coding
CC regions and all segments of RNAs encoding proteins associated with one
CC or more diseases, conditions or mixtures. The antisense oligonucleotides
CC may be derived from sequences X55272-74. These multiple target
CC oligonucleotides (specifically X55180-271) can be used for the antisense
CC treatment of diseases and conditions. Typical diseases and conditions
CC are those associated with impaired respiration and inflammation,
CC including lung diseases, pulmonary vasoconstriction, inflammation,
CC allergic rhinitis, acute asthma, allergies, asthma, impeded respiration,
CC respiratory distress syndrome, pain, cystic fibrosis, pulmonary
CC hypertension, pulmonary vasoconstriction, emphysema, chronic obstructive
CC pulmonary disease (COPD), and cancers such as leukemias, lymphomas,
CC carcinomas e.g. colon cancer, breast cancer, lung cancer, pancreatic
CC cancer, hepatocellular carcinoma, kidney cancer, melanoma, hepatic
CC metastases, as well as all types of cancers which may metastasize or have
CC metastasized to the lungs, including breast and prostate cancer.
SQ Sequence 114955 BP; 6071 A; 29417 C; 36712 G; 21328 T;

Query Match 5.1%; Score 70.4; DB 1; Length 114955;
Best Local Similarity 32.7%; Pred. No. 6.5e-06;
Matches 182; Conservative 58; Mismatches 316; Indels 0; Gaps 0;

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Qy     26 CCGCCCGCCGGCTCCCCCTCCCCCGATCCCTCGGGTCCCGGGATGGGGGGGCGGTGAGGC 85
          ||| ||| |||| | |  :  :||  ||  | ||   || |        :|||   |||
Db 105272 CCGGCCGGCGGCGCGCNNHNNNSCGGCCCGGCCGGCGGCGCGCCNNHNNNSCGGCCCGGC 105213

Qy     86 AGGCACAGCCCCCCGCCCCCATGGCCGCCCGTCGGAGCCAGAGGCGGAGGGGGCGCCGGG 145
           |||   || |||  :   :  | ||| ||| ||| ||    :       : ||| | |
Db 105212 CGGCGGCGCGCCCNNHNNNSCGGCCCGGCCGGCGGCGCGCCCVNNHNNNSCGGCCCGGCC 105153

Qy    146 GGGAGCCGGGCACCGCCCTGCTGGTCCCGCTCGCGCTGGGCCTGGGCCTGGCGCTGGCCT 205
          ||  ||  | | :   :   : || || ||  |||  | ||| :||  :   :| | ||
Db 105152 GGCGGCGCGCCCVGNNHNNNSCGGCCCGGCCGGCGGCGCGCCCVGGNNHNNNSCGGCCCG 105093

Qy    206 GCCTCGGCCTCCTGCTGGCCGTGGTCAGTTTGGGGAGCCGGGCATCGCTGTCCGCCCAGG 265
          |||   | | |   | |||  :   : |    ||  | |||    | | | ||  :  :
Db 105092 GCCGGCGGCGCGCCCVGGCNNHNNNSCGGCCCGGCCGGCGGCGCGCCCVGGCCNNHNNNS 105033

Qy    266 AGCCTGCCCAGGAGGAGCTGGTGGCAGAGGAGGACCAGGACCCGTCGGAACTGAATCCCC 325
           | |    | || || ||    :|   :  :   :| |  |      |   |      |:
Db 105032 CGGCCCGGCCGGCGGCGCGCCCVGGCCVNNHNNNSCGGCCCGGCCGGCGGCGCGCCCVGG 104973

Qy    326 AGACAGAAGAAAGCCAGGATCCTGCGCCTTTCCTGAACCGACTAGTTCGGCCTCGCAGAA 385
            :   :     | |  |  |    ||    || |  |:|   :   :  | | ||
Db 104972 CCVGNNHNNNSCGGCCCGGCCGGCGGCGCGCCCVGGCCVGCNNHNNNSCGGCCCGGCCGG 104913

Qy    386 GTGCACCTAAAGGCCGGAAAACACGGGCTCGAAGAGCGATCGCAGCCCATTATGAAGTTC 445
           || |    :||||:|    :   :|  |:  |       :: |||:      :    |
Db 104912 CGGCGCGCCCVGGCCVGCGNNHNNNSGGCCVGCGGNNHNNNSVGGCCVGCGGNNHNNNSC 104853

Qy    446 ATCCACGACCTGGACAGGACGGAGCGCAGGCAGGTGTGGACGGGACAGTGAGTGGCTGGG 505
          :  | :|     :  :||  :|| |  :   :   : | :  |       :
Db 104852 VGGCCVGCGGNNHNNNSCCVGGCCVGCGGNNHNNNSCCCVGGCCVGCGGNNHNNNSGCCC 104793

Qy    506 AGGAAGCCAGAATCAACAGCTCCAGCCCTCTGCGCTACAACCGCCAGATCGGGGAGTTTA 565
          :||  : | |  :   : || |: |||: | |  :      |  ||:|  |:| |   :
Db 104792 VGGCCVGCGGNNHNNNSCGCCCVGGCCVGCGGNNHNNNSGCGCCCVGGCCVGCGGNNHNN 104733

Qy    566 TAGTCACCCGGGCTGG 581
            | |||:||| :|
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